Title: Development of a Common Biospecimen Coordination System and Informatics Infrastructure for NCI Prostate Specialized Programs of Research Excellence (SPOREs)

INTRODUCTION

Objective

The objective of this contract is to develop a design plan (with budget) and implement a pilot system to establish a common biospecimen coordination system and informatics infrastructure (the "Biospecimen Coordination System") for multiple NCI SPOREs in prostate cancer research. This system will facilitate biospecimen and data sharing among scientific investigators located at different institutions by supporting the use of standardized approaches for collecting, processing, storing, annotating and distributing high-quality biospecimens. Initially, this system will support the Inter-SPORE Prostate Biomarkers Study (IPBS), a validation study of prospective prostate cancer biomarkers. Ultimately, the purpose of this project is to serve as a pilot for the evolving National Biospecimen Network (NBN) by developing an infrastructure to annotate and integrate specimen banks, such as those of the SPOREs, to enhance the quality and availability of various biospecimens and associated data for the broader scientific community.

To accommodate the complexity of designing and implementing such a novel Biospecimen Coordination System and supporting informatics infrastructure, this contract consists of two phases:

*Phase 1 focuses on developing a design plan and budget for system implementation. In addition to developing a recommended implementation strategy, the Phase 1 design plan shall describe two (2) other viable options and alternatives for implementing the pilot system and provide a detailed budget for each option/alternative system implementation. The Contractor shall submit the recommended design plan and two (2) viable alternatives or options within 90 days of the contract award. The Contractor shall respond to questions from an NCI-convened expert review committee for approximately 30 days after submission of the design plan and two (2) viable alternatives or options.

*Phase 2, the implementation of a pilot system for the Prostate SPOREs, will be contingent upon review and approval of the Phase 1 design plan by the NCI-convened expert committee. The expert review committee may accept the Phase 1 design plan, reject the Phase 1 design plan, or recommend changes based upon the options and alternatives stated in the design plan. An important charge of the expert review committee will be to determine the appropriate human subject provisions for Phase 2 based on the accepted/approved Phase 1 design plan. The Contractor shall incorporate and implement all required human subjects requirements, if any. Therefore, Phase 2 is an option to be exercised at the discretion of the Government. The period of performance for Phase 2 is twenty (20) months. The overall scope of work, milestones, and deliverables for Phases 1 and 2 are described in the following sections.

If the pilot project is successful, then the government intends to use the Biospecimen Coordination System developed by the Contractor for other NCI and government projects. Future acquisitions to use, modify and/or update the Biospecimen Coordination System for other government projects will be awarded on a competitive basis.

Background

The deciphering of the human genome greatly increases the opportunities for translational research, offering insight into the development of numerous therapies, predictors, and markers for cancer. When combined with accurate analytic methods, the study of carefully prepared and highly annotated human biospecimens with detailed clinical information offers an unprecedented opportunity for the robust identification and accurate quantitation of molecular signatures of cancer, thereby accelerating the development and implementation of new cancer markers and therapies. While a growing array of new technologies offers increased speed and opportunities for multiplex analyses, they also expose a pressing need for high-quality biospecimens and integrated data banks that can support large-scale population-based research and clinical studies. Several large-scale "biobanks" have emerged in the United States and abroad in the last few years,[1-4] but many technical, logistical and policy issues must be resolved to realize the full potential of such resources.

Over the past several years, leaders from all sectors of the cancer research community have consistently identified the lack of appropriately collected and annotated tissue as a significant barrier to capitalize fully on advances in genomic and proteomic technologies for the prevention, diagnosis, and treatment of cancer.[5-9] High-quality biospecimens with detailed clinical information are needed to conduct translational research to develop meaningful molecular profiles to classify, monitor, and characterize many types of cancer. In recent decades, molecular profiles have become increasingly integrated into standard patient care. However, despite the accelerated rate of tumor marker discovery, the rate of implementation of new markers has been limited, largely due to a lack of appropriate human specimens for robust test development. Our ability to generate high-quality data from biospecimens and clinical information is contingent on rigorous procedures that enable the development of an accurate and reproducible molecular-based taxonomy for cancer, create new targeted therapies, identify new uses for existing targeted drugs, and usher in an era of personalized medicine. Properly annotated biospecimens and associated clinical data will play pivotal roles in accelerating oncology drug development, as the successful identification and credentialing of drug targets and confirmation of diagnostic biomarkers often depends upon connecting biospecimens with clinical information at initial presentation and throughout the course of disease.[10]

Large, statistically powerful cross-institutional datasets are needed to support hypothesis generation and validation of promising diagnostic, prognostic and predictive biomarkers. As the abundance of research and clinical data and the level of detail about the molecular/cellular classification of disease increase, the sharing of data and resources becomes more critical to accelerate progress against cancer. Accessible community cancer databases, such as the Oncomine cancer microarray database (http://www.oncomine.org) hosted at the University of Michigan, are growing in popularity. Moreover, the NIH has instituted a Data Sharing Policy

(http://grants.nih.gov/grants/policy/data_sharing/ and http://grants.nih.gov/grants/policy/model_organisms/) to encourage researchers to make available data and results of benefit to the larger research community. Recognizing the central role of bioinformatics in the post-genomic era, the NCI is currently developing the Cancer Biomedical Informatics Grid (caBIG; http://cabig.nci.nih.gov), a voluntary virtual network of cancer and biomedical researchers who share data and resources based on common data standards and open source principles. CaBIG features a shared vocabulary, data elements, and data models and a collection of interoperable applications developed to a common standard to enable the mining and integration of published cancer research data, principles that will be critical to the success of developing a common biospecimen coordination system and informatics infrastructure for the NCI Prostate SPOREs.

Despite increased community awareness of the importance of sharing data and resources, technical, logistical and policy barriers continue to restrict cancer researchers from realizing the full potential of archived biospecimens and related data. A 2003 monograph from the RAND Corporation,[1] Case Studies of Existing Human Tissue Repositories: "Best Practices" for a Biospecimen Resource for the Genomic and Proteomic Era (http://www.rand.org/publications/MG/MG120/), surveyed 12 existing biorepositories, demonstrating wide variations in protocols for biospecimen collection, processing, annotation and storage, and non-uniform bioinformatics systems. Reports in the literature suggest that specific procedural details, such as the length of time between surgical excision and specimen freezing,[11-13] conditions of tissue fixation,[14] and sample storage,[15] can impact the measurement of gene expression patterns, and a variety of biomarkers. Therefore, developing reliable standard operating procedures (SOPs) for collection, processing, annotation, storage, and dissemination will allow accurate comparisons of data derived from biospecimens collected at different institutions.[16] The detailed annotation of specimen processing variables will also enable determinations of the effects of preanalytic confounders on specimen analysis, thereby enabling the development of standard operating procedures for robust single analyte and multiplex testing.

Heightened concerns about patient privacy in the post-genomic era pose another barrier to sharing biospecimens and associated data, as many biorepositories impose a variety of access restrictions and create localized patient consent procedures that may hinder the dissemination of biospecimens for research purposes. Although population-based projects such as the Marshfield Clinic Personalized Medicine Research Project in Wisconsin (http://www.mfldclin.edu/pmrp/default.asp) and the proposed CARTaGENE project in Quebec (www.cartagene.qc.ca/en) have emphasized the need to foster public understanding of biorepositories, many obstacles remain with regard to garnering the public's trust.[17]

The protection of human subjects, data privacy, and ethical issues associated with biomedical research entail a complicated process with many interlocking steps. To overcome challenges associated with this process, a chain of trust must be established throughout the system that begins with the patient and extends to each individual scientist and professional who uses biospecimens in research. Establishment of secure data systems, harmonization of informed consent policies and procedures, and clearly-defined operating procedures will enable this

chain of trust and accelerate the education of the public regarding the benefits and value of donating their biospecimens for research.

To assist in overcoming barriers and establishing a chain of trust, the NCI seeks to develop new infrastructures to support the coordinated management of biorepositories across different laboratories and institutions using the principles outlined in the National Biospecimen Network (NBN) Blueprint (http://www.ndoc.org/about_ndc/reports), developed by leaders in the cancer research community.[18] The NBN Blueprint outlines a concept for a national, "best practices"-based tissue resource to manage the standardized collection, processing, storage and distribution of high-quality biospecimens and linked data to support and reduce variability in translational research. An integrated biospecimen coordination system such as that outlined in the NBN Blueprint, will increase access to biospecimens and data while concurrently streamlining the collection of these data from existing resources.[19] The group of experts that developed the NBN Blueprint suggested initiating pilot efforts to begin to create an in silico research resource, where scientists can interrogate data about biospecimens without requiring access to the physical biospecimens themselves. This contract supports one such pilot project, the development of a common biospecimen coordination system and informatics infrastructure to support collaborative projects related to prostate cancer research currently underway at participating Specialized Programs of Research Excellence across the nation.

The NCI Specialized Program in Research Excellence (SPORE) in Prostate Cancer

Background of SPORE Initiative. In 1992, the NCI established the Specialized Programs of Research Excellence (SPOREs; http://spores.nci.nih.gov) to promote interdisciplinary research and accelerate the exchange of information and ideas between basic and clinical scientists focused on site-specific cancers. The SPORE program seeks to bring novel ideas to clinical care settings that have the potential to reduce cancer incidence and mortality, improve survival, and enhance patient quality of life. SPORE laboratory and clinical scientists collaborate to plan, design and implement research programs that impact cancer prevention, detection, diagnosis, treatment and control. To facilitate this research, each SPORE develops and maintains resources that benefit all scientists working on the specific cancer site, as well as SPORE scientists.

SPOREs meet at least twice per year to share data, assess research progress, identify new research opportunities and establish priorities for research most likely to reduce incidence and mortality and to increase survival. Currently, the NCI funds 58 SPOREs for 14 organ sites; 11 of these funded SPOREs focus on prostate cancer research (Baylor College of Medicine, Dana Farber/Harvard Cancer Center, Johns Hopkins School of Medicine, Mayo Clinic, M.D. Anderson Cancer Center, Memorial Sloan-Kettering Cancer Center, Northwestern University, University of Michigan, University of California San Francisco, University of California Los Angeles, University of Washington/Fred Hutchinson Cancer Research Center).

The Inter-SPORE Prostate Biomarkers Study (IPBS). The IPBS was conceived by the Prostate SPOREs as an approach to develop an integrated system to validate new biomarkers for prostate cancer. After several planning meetings, individual Prostate SPORE programs submitted proposals for testing candidate biomarkers that could provide accurate prognostic and predictive information about prostate cancer. By developing a system to evaluate these candidate biomarkers, the IBPS will allow the Prostate SPOREs to develop a common platform for conducting translational research.

While prostate-specific antigen (PSA) has been widely used in the clinical management of prostate cancer,[20] the prognostic significance of PSA-defined recurrence following definitive surgery or radiotherapy remains unclear.[21-23] Prostate SPORE investigators have developed the most commonly used nomograms for prostate cancer, including pre-operative clinical information (such as serum PSA level and Gleason grade) and post-operative pathological data. While these nomograms remain informative, SPORE researchers are now incorporating molecular profiles into current clinical models of disease risk to improve the monitoring of both disease and risk. Several promising molecular prognostic biomarkers for prostate cancer have been evaluated in discrete studies, suggesting that a larger comparative study is warranted. Unfortunately, the full translation of promising biomarkers for use in prostate cancer clinical decision making has been hampered by numerous factors, including inconsistent results, the use of smaller retrospective studies, and a lack of validated and rigorous methods and protocols for sample collection, annotation, collection, processing, and utilization.

The purpose of the IPBS is to rigorously and systematically evaluate eight specific promising candidate biomarkers for prognosis following definitive therapy (e.g., radical prostatectomy (RP) or external radiation therapy (XRT)). Five biomarkers will be evaluated through a multi-institutional Inter-Prostate SPORE prospective study. All of the candidate biomarkers are currently under development in the various Prostate SPOREs, and the IPBS is designed to advance selected biomarkers toward clinical use. To evaluate their utility, prognostic biomarkers will be correlated with biochemical recurrence, rapid doubling time and the development of distant metastases. It is anticipated that the outcome of this study will lead to 1) elucidation of novel molecular information regarding prostate cancer progression; 2) stratification of patients regarding outcome following RP or XRT; 3) determination of a biomarker(s) profile that will inform specific experimental neoadjuvant therapies; and 4) identification of novel drug/gene targets.

Building upon SPORE expertise in collecting samples for translational research, the IPBS serves as a pilot study to test the infrastructure, procedures, and resources that will be necessary to establish a National Biospecimen Network.[18] The process of implementing the IPBS and evaluating the effectiveness of its protocols, infrastructure, and mechanisms to collect and distribute biospecimens and data will serve as a pilot test for elements critical to the NBN. Specifically, the IPBS will establish a resource of well-characterized tissue, blood products (including serum and plasma), urine, and other bodily fluids linked to clinical and epidemiological data for future biomarker discovery and validation. In doing so, the

performance of critical elements of the IPBS, such as standardized protocols for sample handling and processing, sample and clinical annotation, biospecimen storage and dissemination, governance and prioritization of access to specimens in the Biospecimen Coordination System, and a bioinformatics infrastructure will serve as pilot tests of components specified in the NBN Blueprint. A synopsis of the IPBS study protocol will be available at the time of the pre-proposal conference for this RFP. The Contractor shall receive a copy of the complete IPBS study protocol upon contract award to ensure that the biospecimen coordination system and informatics infrastructure are tailored to the needs of the IPBS study.

To achieve the goals of the IPBS, the participating Prostate SPOREs intend to develop a common Biospecimen Coordination System and informatics infrastructure that links the participating sites, a goal for inter-SPORE collaboration since the inception of the SPORE program. The informatics infrastructure will promote communication and the exchange of samples and data between participating centers and will be fully compatible with caBIG (caBIG compatibility guidelines are available at http://cabig.nci.nih.gov/guidelines_documentation/caBIG_Compatibility_Document). Thus, in addition to serving as a pilot for the NBN, the IPBS infrastructure will provide the Prostate SPOREs with an integrated, scalable bioinformatics network that could serve as a model for other organ sites.

Based on results from preliminary site visits and surveys, significant variability exists in the bioinformatics and annotation systems at the participating Prostate SPOREs. For example, informatics capabilities range from Excel spreadsheets that include patient identifying information to sophisticated, n-tiered systems that track individual consents and manage biospecimens from hundreds of clinical trials. To develop a bioinformatics infrastructure that incorporates and augments the capabilities of the existing systems, the Contractor shall build upon the work of the initial site visits but are advised to identify and consult with all relevant stakeholders at each participating institution. Each participating institution has an NCI-funded tissue bank(s), some of which are connected through cooperative virtual tissue resources, such as the Cooperative Prostate Cancer Tissue Resource (CPCTR), the Early Detection Research Network (EDRN), or the Cooperative Human Tissue Network (CHTN). One of the objectives of this contract will be to draw from the strengths of the CPCTR, EDRN, and CHTN and other existing systems to transform these isolated or partially-integrated SPORE tissue banks into a more integrated system to enhance the value of the existing resources. Finally, the common biospecimen coordination system and informatics infrastructure that will be developed through this contract must be designed in a manner that does not disrupt the existing workflow in pathology departments.

Biospecimen Coordination System Governance and Oversight

A Prostate SPORE Task Force for NBN Implementation has been assembled by the Principal Investigators of the Prostate SPOREs to assist the Contractor in developing the Common Biospecimen Coordination System. The Contractor will work closely with this Task Force during both phases of the project. In addition, a Governance Board will be formed to oversee

operations of the Biospecimen Coordination System. After achieving the goals of the IPBS study, the Biospecimen Coordination System will make biospecimens and associated clinical information available among the scientific community, including investigators outside of the Prostate SPOREs. First priority for biospecimens collected will be for the IPBS study and a Subcommittee of the Governance Board, the Biospecimen Utilization Subcommittee (BUS) will review requests for use of biospecimens and associated data for funded, Institutional Review Board (IRB)-approved studies (see below for more information about the BUS). In addition to providing access to biospecimens and data through the BUS, the Biospecimen Coordination System will also offer centralized, public access to published data derived from the biospecimens collected in support of the IPBS and other approved studies.

The Governance Board is the governing body of the Biospecimen Coordination System. The Governance Board will advise the NCI Project Officer about working with the participating Prostate SPORE programs, and will review the plans for the Biospecimen Coordination System established by the Contractor. The Governance Board serves a critical advisory role for the project; however, the NCI Project Officer will be responsible for final approval of all work performed by the Contractor. In accordance with the terms of this contract, the Governance Board will communicate directly with the Contractor's Project Manager via the NCI Project Officer.

The Governance Board will consist of four PIs from each participating Prostate SPORE program, an NCI representative, a representative from the NCI Advisory Boards and other ad hoc experts. The NCI Project Officer will participate as a non-voting member of the Governance Board. The Governance Board will meet several times a year and arrange conference calls as necessary. These meetings will help coordinate the activities of the participating laboratories, establish new policies and priorities, and review progress of the Contractor and participating SPORE programs. At its initial meeting, the Governance Board will elect a chairperson (who cannot be the NCI Project Officer). The Chair is responsible for coordinating the Board activities, for preparing meeting agendas, and for scheduling and chairing meetings.

The Prostate SPORE representatives to the Governance Board will provide regular progress updates about the initiative to the NCI Advisory Boards. The purposes of these briefings are to ensure coordination with related NCI activities and ensure that key findings from this initiative are shared with other NCI-supported programs that collect, store, and distribute human biospecimens for research purposes.

The Biospecimen Utilization Subcommittee (BUS) is an independent group of experts that will be constituted by the NCI in consultation with the Governance Board. The BUS is responsible for reviewing requests from investigators for biospecimens unused by the IPBS. In addition to prioritizing requests for biospecimens through an efficient, scientific peer-review process, the BUS will also review requests from researchers who seek only to obtain access to (de-identified) demographic and clinical information collected about the biospecimens. Access to published research results derived from biospecimens collected by the Biospecimen Coordination System will be publicly available through a common database developed by the Contractor (see below).

The NCI will designate a representative to the BUS. This representative, who cannot be the NCI Project Officer nor chair the BUS, is a member of the BUS and participates in developing recommendations to the Governance Board about the scientific importance of proposed assays and the design of proposed studies. The composition and expertise of the BUS will be determined initially by the Governance Board. BUS members must have appropriate expertise in prostate cancer and might include clinicians, laboratory researchers, statisticians, patient advocates, ethics experts, and members with other expertise suggested by the Governance Board. Two members of the Governance Board may serve as ad hoc non-voting members of the BUS.

The establishment of the BUS for the Biospecimen Coordination System reflects the 2001 NCI guidelines for Shared Resources or Cores within the SPOREs (http://spores.nci.nih.gov/guidelines/guidelines_full.html). These guidelines specifically state that:

> *"Each SPORE must have a dedicated component for collecting and distributing human cancer site-specific tissue. The tissues may be frozen or archived paraffin blocks, slides, or fluids such as serum, plasma, urine, or sputum samples. This shall be a true tissue resource that can be used to generate and test translational hypotheses, rather than a small collection of heterogeneous samples. The tissue core shall also include the essential pathological, clinical and family history information needed for conducting a wide range of translational research. Appropriate informatics capability for tracking, as well as linkage to clinical and follow-up data sets, shall be demonstrated.*
>
> *This resource shall benefit the specific research activities of the SPORE, as well as the research activities of other scientists within and outside the parent institution who are concentrating on translational research issues. A plan must be proposed for prioritizing distribution of tissues to SPORE scientists and others based on the merit of translational cancer research projects."*

Biospecimen Coordination System Components and Requirements

The Biospecimen Coordination System described here is not intended to supplant existing resources at the participating SPORE sites, but rather to integrate them to fill a need not served by current resources. Furthermore, the Biospecimen Coordination System must be designed to integrate with surgery, pathology and other clinical departments without interrupting existing workflows.

The major components of the Biospecimen Coordination System include:

a. Human subjects protection, privacy protection and informed consent processes
b. Rigorous standard operating procedures for biospecimen collection, processing, annotation, storage and dissemination
c. Quality assurance/quality control
d. Integration with associated clinical data, both retrospectively and prospectively

e. Informatics system requirements
f. Biospecimen and data access policies
g. Biohazard considerations and packing, shipping and storage policies
h. Intellectual property/Ongoing system oversight and maintenance
i. Establishment of a common repository for biospecimens unused by the IPBS
j. Personnel management

Detailed requirements in each of these areas are addressed below.

Human Subjects Protection, Privacy Protection and Informed Consent Processes. The Contractor will not interface directly with patients, nor use the biospecimens and data collected for research purposes; however, the Contractor shall assist the Prostate SPOREs in developing a harmonized, coordinated approach for addressing human subjects protection, privacy protection, and the informed consent process. Harmonization of these processes and protocols is central to a successful plan for a Biospecimen Coordination System. Therefore, the Contractor will work with the Prostate SPOREs to develop a Biospecimen Coordination System that shall:

a. Conform to all relevant human subjects regulations including 21 CFR 50 and 45 CFR 46.
b. Conform to all Federal and state privacy regulations including the HIPAA Privacy Rule (see http://privacyruleandresearch.nih.gov/)
c. Conform to requirements established by the Institutional Review Boards (IRBs) affiliated with the participating Prostate SPORE programs.
d. Feature a harmonized consenting process (ideally including a common consent form) for all participating programs. This process shall adhere to the highest ethical and legal standards and establish a chain of trust throughout the biospecimen coordination system that begins with the patient and extends to each individual scientist who uses biospecimens for research.
e. Address the future use of Biospecimen Coordination System materials beyond the IPBS; e.g., examine local, state, and Federal regulations to create informed consent forms that enable future use of Biospecimen Coordination System biospecimens for genomic or proteomic studies.

Standard Operating Procedures for Biospecimen Collection, Processing, Annotation, Storage and Dissemination. A preliminary analysis of the participating Prostate SPOREs indicates that procedures for collecting, processing, annotating, and storing biospecimens differ among these programs. Therefore, the Biospecimen Coordination System shall employ a set of “best practices”-based standard operating procedures (SOPs) developed in collaboration between the Contractor, the participating Prostate SPORE programs and the NCI. In situations where complete standardization is not possible, detailed information will be maintained about the collection procedures employed. The system will also include provisions for revising and updating these procedures. These SOPs shall be based on common requirements that reflect relevant institution-specific capabilities and needs.

The Biospecimen Coordination System shall address, but is not limited to, the specific issues listed below. Additional parameters for biospecimen handling beyond those outlined here may be included as appropriate.

a. Collection of paraffin-embedded tissue, fresh-frozen tissue, blood (including serum and plasma) and urine samples. Biospecimens collected for the IPBS study will be stored locally at each individual Prostate SPORE program; however, some remaining biospecimens will be transferred to a common repository managed by the Contractor. This common repository will include an infrastructure to ship and transfer samples easily among participating SPORE programs and outside scientific investigators. SOPs for biospecimen collection, processing, annotation, storage, and dissemination shall address many parameters, including:
   (1) Dates of sample acquisition, processing, and storage
   (2) Temperature of sample prior to processing
   (3) Surgical procedure
   (4) Time between stoppage of circulation to tissue and tissue excision
   (5) Time from sample acquisition until processing
   (6) Temperature and duration of all processing steps, including paraffin temperature during embedding
   (7) Storage temperature
   (8) Time between sample collection and initiation of processing
   (9) Time of fixation, dehydration, clearing and infiltration (embedding)
   (10) Method of sample acquisition (including type of preservative for blood samples)
   (11) Size or volume of sample and the number of slides, blocks, or aliquots
   (12) Sectioning of diagnostic and research sections
   (13) Type of slide
   (14) Slide storage conditions
   (15) Type of tube and preservative
   (16) Centrifuge speed (in g-force) and time for serum and plasma biospecimens
   (17) Volume and number of aliquots of fluid specimens
   (18) Cell count of cellular specimens
   (19) Volume/weight of solid tissue specimens
   (20) Freeze-thaw cycles, dates, and times
   (21) Amount of sample dispersed and to whom

b. Provisions to track heterogeneous collection methods where complete standardization is not possible.

c. Relevant demographic, pathologic and clinical annotation (see below for details) that will be tracked, managed and stored in a common informatics platform, but not necessarily in a central database.

d. Verification that specimens required for the IPBS will be available from the participating programs during the timeframe for implementing the system.

Quality Assurance (QA) and Quality Control (QC). A process shall be established to periodically verify the quality of biospecimens collected for the Biospecimen Coordination System to ensure that they are suitable for high-throughput genomic and proteomic research (e.g., analyzing DNA and RNA integrity using an Agilent 2100 Bioanalyzer or other methods). In addition, a parallel process will monitor the quality of all data collected about the biospecimens.

Integration with Associated Clinical Data. Participating SPOREs will also collect and record clinical data relevant to the IPBS study to determine the prognostic and predictive value of the prostate cancer biomarkers under investigation. Such data may include, but is not limited to:

a. Pre- and post-treatment serum chemistry (including PSA levels)
b. Gleason scores (biopsy and/or pathology)
c. Clinical and pathological stages of disease
d. Extent of tumor in biopsy
e. Demographic information (e.g., age, ethnicity, family history)
f. Five-year probability of freedom from biochemical recurrence (nomograms)
g. Radiographic evidence of disease stabilization or regression
h. Duration of response (e.g., time to further progression)
i. Specific aspects of treatment procedures (e.g., type of surgery performed, radiation dose)
j. Pre-surgery biopsy with Gleason score, core details and results
k. Pre-surgery transrectal ultrasound (TRUS)
l. Radical prostatectomy (RP) pathology (e.g., extracapsular extension, seminal vesicle invasion, surgical margin, surgeon, date of surgery, Gleason score, path sections and findings)
m. Pelvic lymph node dissection (PLND)
n. Annual post-surgery PSA measurements
o. Concomitant medical therapies and medications

The informatics system (described below) should allow for the exchange of such clinical data between participating sites.

Informatics System Requirements. The Contractor shall work with the Prostate SPORE NBN Pilot Task Force Informatics Group to develop an interoperable informatics system that will exchange clinical and biospecimen data between sites in the format of a core of common data elements (CDEs), which will include key demographic, clinical, pathology, specimen processing, and specimen inventory variables that are represented in a similar format by a majority of prostate cancer researchers. Algorithms and database queries will translate data elements that vary among SPORE sites to the common format (e.g., XML) and assemble them for compliance and efficient exchange. Biospecimen and patient data not represented by the CDEs will remain in the databases of the individual SPOREs but can be compiled by the

centralized interoperability layer to form a virtual multi-center database. The final product of such a system will be a searchable web catalog of data and biospecimens, supported by a regulatory-compliant exchange infrastructure for requests or distribution.

The informatics infrastructure will serve the needs of the IPBS, will provide the basis for supporting a more generalized inter-Prostate SPORE research infrastructure, and will be compatible with the context of existing systems at the participating Prostate SPOREs. The key requirements for the bioinformatics system are flexibility, i.e., the ability to communicate with information systems already in place at the SPOREs, and scalability; i.e., the initial implementation specific for prostate cancer must be readily adaptable to other organ sites and retain the ability to add new data structures in a transparent fashion.

Each of the informatics systems described below shall be based on a set of Common Data Elements (CDEs), be caBIG-compatible, and have querying capabilities. Because these systems will be built upon existing CDEs, the Contractor shall review the CDE experience of relevant models, such as the NCI''s Early Detection Research Network (EDRN),[24] and other tissue repository networks. In addition, the NCI Cancer Data Standards Repository (caDSR) (http://ncicb.nci.nih.gov/core/caDSR) will serve as the metadata repository. All CDEs will be constrained by standardized terminology included in the NCI Enterprise Vocabulary Services (EVS) (http://ncicb.nci.nih.gov/core/EVS).

The informatics system must comply with caBIG infrastructure and architecture, including consistency with caCORE, APIs, EVS, caDSR, and the caCORE common security module. As described at http://cabig.nci.nih.gov/guidelines_documentation/caBIG_Compatibility_Document, caBIG compatibility assumes an open-source, open-access, open-development, and federated model. The caBIG guidelines describe a range of maturity levels (e.g., “legacy,” “bronze,” “silver,” and “gold”) to characterize the compatibility of various software application components (e.g., data elements, interface integration, vocabularies and terminologies). While site-specific databases at individual Prostate SPORE programs may attain differing maturity levels, the interoperability layer developed by the Contractor shall meet at least the "silver" level of caBIG compatibility.

The informatics system described here shall align with the principles of the caBIG Tissue Banks and Pathology Tools Workspace (http://cabig.nci.nih.gov/workspaces/ws3), which provides for the implementation and integration of tissue bank and pathology tools and infrastructure components that facilitate information sharing. To avoid duplication of effort, the Biospecimen Coordination System shall directly incorporate tools developed by the caBIG Tissue Banks and Pathology Tools Workspace (and other relevant caBIG Workspaces) whenever possible.

a. The interoperability layer for the Biospecimen Coordination System informatics System shall feature:

(1) A Clinical Data System to record a set of CDEs that comprehensively describes a prostate cancer biospecimen. This system, or coordinated

combination of systems, must track clinical information associated with a biospecimen across multiple departments including Urology, Medical Oncology and Radiation Oncology. The system shall also assure adequate longitudinal follow-up of patients, as well as completeness and quality of CDEs.

(2) A Protocol Management System to track each step of the IPBS, at the level of an individual participating program (for use by a research assistant or study nurse) and across programs from multiple institutions (for use by inter-site coordinators). The system must track protocol screening and itemized consents, completed and pending data collection, collection of biospecimens, and longitudinal follow-up data.

(3) A Biospecimen Tracking System to track the location, processing, quality control and distribution of each biospecimen collected. The biospecimen tracking system shall record each processing step, quality control check, the physical location, amount, and distribution plans for each sample. The CDEs that describe the histopathology of each sample shall accompany the biospecimen, and the biospecimen tracking system shall record the rules for using particular samples (i.e., reserving them for a particular study protocol.) It must also have capabilities to manage the shipping and distribution of biospecimens to investigators at participating SPOREs and to researchers outside the SPORE network. The biospecimen tracking system must conform to International Air Transport Association (IATA) standards for air shipments and U.S. Department of Transportation standards for domestic ground shipments and guarantee packing conditions appropriate to protect samples from temperature variations during transit.

(4) A Results Bank to store and share all published research results (including results from the IPBS) derived from biospecimens collected for the Biospecimen Coordination System.

b. The exchange of information among the Prostate SPORE programs through the interoperability layer shall be an automated, labor-free process that is based on common data exchange standards, and should facilitate sharing and comparing results from the IPBS by developing the following features:

(1) A web interface and portal that features both password-protected (a searchable catalog accessible to any authorized investigator) and general access sections (a publicly available database that includes all published research results of analyses derived from biospecimens collected by the Biospecimen Coordination System, basic inventory information and a description of how to apply for access to biospecimens and data through the Biospecimen Utilization Subcommittee)

(2) The ability to archive and share data from single analyte and multiplex analyses (e.g., immunohistochemical (IHC) data, expression arrays) and clinical data in a consistent manner to facilitate information sharing among the participating Prostate SPORE sites
(3) A biospecimen tracking system that records processing, storage, requests, shipments, and receipts, and the transmission of histopathological and processing CDEs among collection sites. Such a system shall be capable of recording an ""electronic audit trail"" that details all alterations, additions, deletions, and adjustments to the data and biospecimens as they are processed and used.
(4) The ability to monitor patient accrual and study progress in real time
(5) Standard interfaces between site-specific protocol management systems and the central protocol coordinating system
(6) A clinical annotation system that facilitates exchange of clinical datasets in CDE format and can attach clinical CDEs to the histopathology, quality assessment, and location-tracking CDEs of the biospecimen tracking system
(7) A presentation layer and user interface that is standard across all new applications and complies with caBIG standards.

c. System security specifications, including:
(1) Compatibility with security modules under development by the NCI Center for Bioinformatics for caBIG.
(2) Handling of patient identifiers in a HIPAA-compliant manner (for guidance on existing NIH policies on public access to research data, see http://grants2.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm. Information on the HIPAA Privacy Rule can be found at http://www.hhs.gov/ocr/. Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding, and progress of monitoring of grants, cooperative agreements, and research contracts can is available at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html).
(3) Restricting catalog access to authorized investigators (i.e., role-based access)
(4) Restricting data entry to authorized roles
(5) Restricting approval for specimen shipments to authorized roles at each institution.

d. System hosting requirements, including:
(1) A central data cache for the protocol monitor
(2) A central data cache for the searchable web catalog
(3) Local database system requirements
(4) Interfaces between local systems and the central coordinating system

e. Software developed for this project will comply with the caBIO license (http://ncicb.nci.nih.gov/NCICB/core/caBIO/technical_resources/core_jar/license) currently employed by caBIG. An updated version of this license will be available in March 2005. All software developed for this Contract will be licensed using the updated version of the caBIO license. The caBIO licensing model is a Berkley-type (BSD) license, which requires new software developed for the Contract to be open source and to operate as a "stand-alone" product. However, unlike the GNU-style licenses, BSD licenses do not require all software additions and extensions not developed under this contract to be open source.

f. Detailed operating procedures regarding the development of code

g. Compliance with the Title 21 Code of Federal Regulations (21 CFR Part 11; http://www.fda.gov/ora/compliance_ref/part11/) regarding electronic records and signatures and maintaining written standard operating procedures for implementing software updates and modifications.

Biospecimen Access Policies. Because of the finite amount of biospecimens that will be collected for this initiative, as described above, a Biospecimen Utilization Subcommittee (BUS) will establish specific rules and regulations (based on the existing SPORE grant guidelines) for the distribution of biospecimens and data. First priority for biospecimens will be given to address the specific questions of the IPBS, but outside investigators will obtain access to remaining biospecimens by submitting research proposal requests to the BUS. The BUS, which will include the Principal Investigators of the SPOREs plus representatives from the external scientific community, the NCI, and the prostate cancer advocacy community, will employ an efficient peer review process to make recommendations to the Governance Board about biospecimen and data access. Current inventory information for the Biospecimen Coordination System will be available to the BUS, the Prostate SPOREs, and outside investigators through the informatics system. Project management support for the Governance Board and Biospecimen Utilization Subcommittee for this project, as well as assistance to the Governance Board to help implement the suggestions of the BUS, will be provided by the Contractor.

Biohazard Considerations and Packing, Shipping and Storage Policies. Because this contract involves the collection, storage, retrieval, and transfer of human biological materials, the identification of biohazards and the minimization of exposure risk are important considerations for the design plan and implementation of this pilot system.[25] All personnel involved in the handling, packaging and shipping of human biospecimens shall be trained about biosafety concerns and adhere to all relevant regulations such as 29 CFR Part 1910.1030, promulgated by the Occupational Safety and Health Administration (OSHA). Additional information on best practices for the collection, storage, and retrieval of human biological materials used in research is available from the International Society for Biological and Environmental Repositories (ISBER) at http://www.isber.org.

Biospecimens shall be packed appropriately to protect them from temperature variations during transit. This may include the use of insulated packing material, refrigerated gel packs, frozen gel packs, dry ice pellets and/or liquid nitrogen shippers. The shipping and handling of biospecimens must meet Government specifications for packaging, labeling and shipping of such samples. All samples shall be marked with the contract number and Contractor name, and all required materials shall be delivered in immediate usable and acceptable condition. Air shipments shall conform to the International Air Transport Association (IATA) standards, and ground shipments in the United States shall conform to the Department of Transportation (DOT) standards. All personnel involved in the shipping and packaging of human biospecimens shall be properly trained for air and ground shipments of human biospecimens.

All biospecimens shall be stored according to best practices, including continual freezer and refrigerator monitoring, systematic equipment maintenance, emergency preparedness, alarm systems, back-up storage capacity, back-up liquid nitrogen supply and back-up power supply. In addition, storage in the vapor phase is preferred for both safety and preservation reasons. The Biospecimen Coordination System shall also feature a protocol for personnel notification and action in the event of emergency.

Intellectual Property/Ongoing System Oversight and Maintenance. The Biospecimen Coordination System shall feature a plan for system auditing. Intellectual property issues for the Contractor and any proposed Subcontractors regarding biospecimens, associated data and any software developed for the informatics system shall be addressed in detail prior to implementation.

Establishment of a Common Repository for Biospecimens Unused by the IPBS. Because the Biospecimen Coordination System is envisioned as an ongoing resource with broad applicability to the greater scientific community, policies must be established for the management of data and biospecimens once the IPBS has been completed. In particular, a separate, common biospecimen repository of material not required for the IPBS will be established. Access to this biorepository will be governed by the BUS according to the principles described in this announcement. This common repository will obtain material throughout the duration of the IPBS study that is not needed for the specific goals outlined in the IPBS protocol. Prostate SPORE programs will store some material locally. However, each participating SPORE program will ship a subset of samples (collected and annotated rigorously by the participating programs using the SOPs established) to the common repository that will be managed by the Contractor (SPOREs will have flexibility in choosing which particular specimens will be shipped to the common repository). The common biorepository shall be capable of storing samples and archiving data related to:

a. Paraffin-embedded tissue collected using the standard operating procedures, demographic and clinical annotation defined for the project from at least 1000 patients (~100 patients per Prostate SPORE)
b. Frozen tissue collected using the standard operating procedures, demographic and clinical annotation defined for the project from at least 1000 patients (~100 patients per Prostate SPORE)

c. Serum collected using the standard operating procedures, demographic and clinical annotation defined for the project from at least 1000 patients (~100 patients per Prostate SPORE)
d. Plasma collected using the standard operating procedures, demographic and clinical annotation defined for the project from at least 1000 patients (~100 patients per Prostate SPORE)

Personnel Management. The Biospecimen Coordination System will incorporate a comprehensive personnel management plan that will address ways to engage and utilize existing personnel at the Prostate SPORE programs and other relevant personnel working in the hospitals and Cancer Centers affiliated with the Prostate SPORE programs through subcontracts with the Prostate SPORE institutions.

Milestones and Process Evaluation

Many elements of the Biospecimen Coordination System will be evaluated during the contract performance. Detailed milestones for system implementation will be defined during Phase 1 of the contract through discussions among the Contractor, Prostate SPORE investigators and other representatives, the NCI, and others. The approved milestones for Phase 2 will be incorporated into the contract by modification. For reference, actual milestones for Phase 1 and estimated milestones for Phase 2 are provided in Appendix A, “Milestones for Biorepository Coordination and Informatics Systems, Phases 1 and 2.”

Offerors shall be provided a synopsis of the Prostate SPORE IPBS study protocol at the pre-proposal interest meeting, and the Contractor shall be provided a complete IPBS study protocol upon contract award.

Possible metrics for system milestones include, but are not limited to, the following:

a. Proportion of samples that conform with specified protocols
b. Ease of IRB approval of common consent elements and research protocol template
c. Completeness of annotation required
d. Ability to retrieve data from enrollment sites using the bioinformatics system
e. Transparency of use and comprehensiveness of virtual catalog of specimens
f. Compatibility between user requests and prioritization system for sample access
g. Biomarker assay data retrieved or linked to catalog
h. Average time between sample request and receipt by end user
i. Number of non-Prostate SPORE investigators requesting biospecimens and accessing data from the public research results database.

APPENDIX A: MILESTONES FOR BIOREPOSITORY COORDINATION AND INFORMATICS SYSTEMS (PHASES 1 AND 2)

As noted previously, the Biospecimen Coordination System design and implementation will consist of a two-phase process to accommodate the complexity of designing and implementing such a novel system and supporting informatics infrastructure. The first phase will focus on developing a design plan, followed by a second phase of implementation as a pilot system for the prostate SPOREs. Initiation of Phase 2 is contingent upon review and approval of the plan by an expert committee convened by the NCI.

Actual administrative and technical milestones for Phase 1 and estimated administrative and technical milestones for Phase 2 are provided below. The actual milestones incorporated in the resultant contract may differ from the estimated milestones below based upon the successful Contractor's proposal.

Phase 1 (4 months total –– months 0-4 of contract performance) entails the development of a detailed design plan and budget for a comprehensive Biospecimen Coordination System to connect all participating Prostate Cancer SPOREs.

During the first 90 days after the award, the Contractor shall complete the design plan and two (2) viable alternatives or options that meet specifications outlined in the Scope of Work for this contract. The Contractor shall respond to questions from the NCI-convened expert review committee for approximately 30 days after submission of the design plan and two (2) viable alternatives or options. The detailed design plan and two (2) viable alternatives or options shall achieve at minimum the milestones listed below. Additional milestones may be added based upon the successful Contractor's proposal.

Milestones (months 0-4)

Administrative

a. Develop plan for identifying the relevant stakeholders at each Prostate SPORE program
b. Develop plan for obtaining detailed information about existing policies, procedures and systems at each participating program and affiliated institution(s)
c. Develop case studies modeled on specific participating SPORE programs to demonstrate a detailed understanding of integrating the common biorepository coordination system with all relevant clinical departments
d. Clarify intellectual property and access expectations among participating programs, consultants and Subcontractors, and offer an integrated approach for intellectual property management including the development of material transfer agreements (in accordance with NIH policies) as needed
e. Outline an approach for implementing an integrated biospecimen coordination system for all participating programs
f. Draft a budget for the system, as described in this document.

g. Identify detailed milestones for system implementation (Phase 2) in collaboration with the Prostate SPORE investigators, other SPORE members, NCI scientists, representatives from advocacy organizations, and other experts
h. Provide a plan for working with the individual SPOREs to meet these specific milestones relating to biospecimens and informatics

Technical

a. Create an inventory of existing informed consent processes at participating programs and a process diagram indicating how these policies may be converged to meet the requirements of the Biospecimen Coordination System
b. Create an inventory of existing clinical data systems at participating programs and a process diagram indicating how these systems may be converged to meet the requirements of the proposed Biospecimen Coordination System
c. Create an inventory of existing tissue procurement systems at participating programs and a process diagram indicating how these systems may be converged to meet the requirements of the proposed Biospecimen Coordination System
d. Building on existing information collected through NCI site visits, outline a plan to address informatics components as described in this document, including a draft list of detailed informatics requirements
e. Based on information gathered from participating SPORE programs, outline a plan to establish a common repository for biospecimens unused by the IPBS.

The Contractor shall deliver the design plan within 90 days of the contract award. It is estimated that the NCI-convened expert committee will need approximately 30 days to review the design plan. While the Contractor will not be allowed to implement these plans without approval by a NCI review committee (see below) and the exercising of Phase 2, it is highly recommended to begin preparing for implementation of the system as soon as possible.

Phase 2 (20 months total –– months 5-24 of contract performance) entails implementation of the design plan across the participating Prostate SPOREs following approval of the plan by an NCI review committee.

The Contractor shall provide a plan for working with the individual SPOREs to help meet defined milestones related to all aspects of the Scope of Work. Examples of areas relevant to this contract that will be included in the Phase 1 process evaluation are listed in the section, "Milestones and Process Evaluation."

The Contractor shall provide estimated milestones for Phase 2 in its proposal. Actual milestones for system implementation will be defined during Phase 1 through discussions among the Contractor, SPORE investigators, other SPORE members, NCI scientists and program staff, and other experts and incorporated into the contract by modification. The Contractor shall complete Phase 2 requirements in a total of 20 months following approval of proposal. Estimated milestones toward which the Contractor shall work during this 20-month implementation period are listed below for reference purposes.

Estimated Milestones (months 5 - 12 of contract performance)

Administrative

a. Establish communications with all participating IRBs and develop a harmonized consent process and document for all participating Prostate SPOREs
b. Develop common material transfer agreement for all participating Prostate SPOREs
c. Convene Governance Board
d. Convene Biospecimen Utilization Subcommittee

Technical

a. Establish SOPs in collaboration with participating SPOREs and the NCI
b. Finalize clinical information to be collected with biospecimens
c. Establish CDEs based on the NCI caDSR and the EVS
d. Finalize informatics system requirements

Estimated Milestones (months 12-18 of contract performance)

Technical

a. Begin collecting specimens using SOPs with detailed clinical annotation
b. Implement an interoperable, common informatics system across all participating Prostate SPOREs, including clinical data system, protocol management system, biospecimen tracking system, and common database for research results
c. Begin establishing a separate, common biorepository of material unused for the IPBS

Estimated Milestones (months 18 –– 24 of contract performance)

Administrative

a. Monitor allocation of biospecimens for the IPBS and for deposit in the repository
b. Allocate biospecimens to ten researchers in the broader research community
c. Verify that 200 researchers have accessed the common research results database
d. Begin implementing process for long-term archival and maintenance of data and biospecimens

Technical

a. Complete biospecimen collection and annotation required for IPBS study
b. Begin submitting published data into common research results database

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DELIVERABLES AND REPORTING REQUIREMENTS

Phase 1- Deliverables

1. Written summary of existing clinical data systems at the Prostate SPOREs and a process diagram indicating how these systems can be converged to develop the common Biospecimen Coordination System and informatics infrastructure outlined in the SOW due 90 days after the Contract start date.
2. Written summary of the inventory of existing biospecimen procurement systems at the Prostate SPOREs and a process diagram indicating how these systems can be converged to develop the common Biospecimen Coordination system and informatics infrastructure outlined in the SOW due 90 days after the Contract start date.
3. Written narrative describing the recommended plan for implementing the common Biospecimen Coordination System and informatics infrastructure due 90 days after the Contract start date.
4. At least three written Case Studies modeled on specific prostate SPORE programs to demonstrate a detailed understanding of integrating the common Biospecimen Coordination System with all relevant clinical departments due 90 days after the Contract start date.
5. Detailed budget for recommended plan due 90 days after the Contract start date.
6. Written narrative describing at least two alternative plans for implementing the common Biospecimen Coordination System and informatics infrastructure due 90 days after the Contract start date.
7. Detailed budget for each alternative plan due 90 days after the Contract start date.
8. Detailed milestones for implementation for recommended and alternative plans due 90 days after the Contract start date.
9. PowerPoint presentation to be delivered to the NCI and the NCI-convened expert committee that will approve or disapprove the implementation plan 90 days after the Contract start date. The PowerPoint presentation shall be delivered by e-mail, CD ROM and in hardcopy.
10. Detailed Automated Information Systems (AIS) Security Plan for Phase II is due 90 days after the Contract start date. This AIS Systems Security Plan will specify suitability designation and investigation, confidentiality/non-disclosure agreement, security awareness and training and other relevant components (See http://ais.nci.nih.gov). This AIS Systems Security Plan must be approved by the government before beginning Phase 2 of the project.

Phase 1- Reporting Requirements

1. Monthly progress reports that include information about work progress in relation to milestones. In addition, this report shall include a description of activities during the reporting period, and the activities planned for the ensuing reporting period.

Phase 2-Deliverables

1. Obtain a Certificate of Confidentiality from the NIH for the project (see http://grants1.nih.gov/grants/policy/coc/background.htm) due 5 months after the Contract start date.

2. A written copy of Standard Operating Procedures for biospecimen collection, processing, storage and distribution employed at all Prostate SPOREs and a summary of any differences among sites if complete standardization is not possible due 7 months after the start of the Contract start date.
3. Common consent form approved by all Prostate SPOREs due 7 months after the start of the Contract start date.
4. Common material transfer agreement approved by all Prostate SPOREs due 7 months after the start of the Contract start date.
5. Detailed list of informatics requirements and UML use cases due 7 months after the start of the Contract start date.
6. List of CDEs mapped to existing CDEs included in the NCI caDSR and the EVS due 10 months after the start of the Contract start date.
7. Paraffin-embedded tissue collected using the standard operating procedures, demographic and clinical annotation defined for the project from at least 1000 patients (~100 patients per Prostate SPORE) archived in a common biorepository due 24 months after the Contract start date.
8. Frozen tissue collected using the standard operating procedures, demographic and clinical annotation defined for the project from at least 1000 patients (~100 patients per Prostate SPORE) archived in a common biorepository due 24 months after the Contract start date.
9. Serum collected using the standard operating procedures, demographic and clinical annotation defined for the project from at least 1000 patients (~100 patients per Prostate SPORE) archived in a common biorepository due 24 months after the Contract start date.
10. Plasma collected using the standard operating procedures, demographic and clinical annotation defined for the project from at least 1000 patients (~100 patients per Prostate SPORE) archived in a common biorepository due 24 months after the Contract start date.
11. All software code, object code, software manuals and flow charts for all software developed under the Contract due 24 months after the Contract start date.

Phase 2- Reporting Requirements

1. Monthly progress reports that include information about work progress in relation to milestones. In addition, this report shall include a description of the activities during the reporting period, and the activities planned for the ensuing reporting period.
2. Annual progress report. This report shall include a summation of the results of the entire Contract work for the period covered. An annual report will not be required for the period when the final report is due. A monthly report shall not be submitted when an annual report is due.
3. Annual Technical Progress Report for Clinical Research Study Populations
4. Final Report. This report shall include a summation of the work performed and the results obtained for the entire contract period of performance. This report shall be in sufficient detail to describe comprehensively the results achieved. An annual report will not be required for the period when the final report is due.

LEVEL OF EFFORT

Phase 1:

Labor Category	**Estimated Number of Hours**
Project Director	290
Senior Software Developer – Interoperability System	90
Senior Biorepository Manager	90
Staff Human Subjects and Privacy Official	40
Total Phase 1: 510 hours	

Phase 2:

Labor Category	**Estimated Number of Hours**
Project Director	1,500
Senior Software Developer –Interoperability System	3,000
System Administrator	1,000
Staff User Interface Developer	1,000
Staff CDE Developer/Mapping Consultant	1,350
Senior Biorepository Manager	3,000
Staff SOP Developer/Consultant	1,325
Staff Human Subjects and Privacy Official	500
Staff Technology Transfer Official	40
Total Phase 2: 12,715 hours	